OBJECTIVES: In 2012, ivabradine was centrally approved by the EMA for Chronic Heart Failure treatment. Through ivabradine NICE and HAS decisions analysis, the objective of this policy research is to illustrate the divergence of HTA decisions despite a consistent efficacy, effectiveness and economics information. **METHODS:** NICE and HAS reports were fully reviewed with a focus on decisions outcomes. Then, convergences and divergences between HAS and NICE decisions were highlighted. **RESULTS:** NICE recommended for use ivabradine for patient with NYHA class II to IV with systolic dysfunction, with sinus rhythm with a heart rate ≥ 75 bpm, in combination with standard therapy or when beta-blocker therapy is contraindicated or not tolerated, and with a left ventricular ejection fraction ≤ 35%. Decision made by NICE was mainly based on results of one subgroup defined post hoc on the request of EMA. HAS rated the actual benefit of ivabradine as important for the labelled indication, nevertheless HAS distinguishes 2 subpopulations: one with minor improvement of actual benefit - patient with NYHA class II to III with systolic dysfunction in sinus rhythm with the heart rate ≥ 77 bpm and in which beta-blockers are contraindicated or not tolerated- for the other patients, HAS stated that ivabradine does not provide improvement in actual benefit. HAS based its decision mainly on the results of one subgroup defined a priori in which ivabradine was superior to each individual components of the primary combined endpoint. **CONCLUSIONS:** While EUnetHTA attempts to provide a coordinated opinion on comparative effectiveness, HTA decisions continue to be divergent across Europe. Ivabradine NICE and HAS decisions divergences exemplify once more the inconsistency of HTA decisions and highlight the obstacle for the establishment of a jointed EUHTA body.

PCV168

QUALITY IMPROVEMENT INITIATIVES FOR PATIENTS ON WARFARIN IN PRIMARY CARE

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OBJECTIVES: The primary objective of this study was to report the clinical outcomes, i.e. routine calculation of time in therapeutic range (TTR), bleed events and thromboembolic events for patients on warfarin in a general practice following the introduction of quality improvement initiatives. A secondary objective was to estimate the cost of care of these patients managed from the perspective of the general practice. **METHODS:** Clinical data were analysed annually using a General Practice database, adapted to allow calculation of TTR for all patients prescribed warfarin for the years 2009 (baseline), to 2011 (Year 2). Decision trees were constructed to reflect typical episodes of care for patients with atrial fibrillation (AF). Resource use and unit cost data were applied to each node in the decision tree. The probabilities of events occurring were derived from the literature and expert clinical opinion. A 60% TTR was used as a reference criterion for patient outcomes. Ethical approval for the study was obtained. Analysis was performed in SPSS®. **RESULTS:** The TTR at baseline was 54%, rising to 61% in Year 1 and 63% in Year 2. One patient suffered a haemorrhagic stroke in the baseline year (TTR 71%), and in the same year there were 4 thromboembolic events. No major haemorrhagic or thromboembolic events have been recorded in the follow-up years. The median cost per patient with AF was €276 (using a median of 12 INR tests per annum). **CONCLUSIONS:** The introduction of routine assessment of TTR in the practice has resulted in a significant improvement in care as demonstrated by the rise in TTR values, and adherence to international best-practice criteria. Clinically significant outcomes on patient care are also evident with the absence of major bleed events or thromboembolic breakthrough events. The study highlights the feasibility and benefits of enhanced care at local level.

MENTAL HEALTH – Clinical Outcomes Studies

PMH1

EFFICACY OF LONG-ACTING INJECTABLE ANTIPSYCHOTIC THERAPIES IN MAINTENANCE TREATMENT OF SCHIZOPHRENIA: A MIXED TREATMENT COMPARISON (MTC) OF DOUBLE-BLIND RANDOMIZED CLINICAL TRIALS

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OBJECTIVES: Treatment with antipsychotic medication is an important element of relapse prevention in the management of schizophrenia. However, approximately 50% of patients with schizophrenia miss taking >30% of their medication, therefore the use of long-acting injectable (LAI) formulations is an important option for patients partially or non-adherent to oral formulations. This study aimed to compare LAIs in terms of efficacy and safety. **METHODS:** A systematic literature review in PubMed, EMBASE, Cochrane, PsychINFO and conference abstracts was conducted to identify relevant randomized controlled trials of LAIs in maintenance treatment in schizophrenia. Selection criteria included long-term follow-up, stable patients and minimamilly one LAI treatment arm. The primary efficacy outcome was relapse rate; rate of discontinuation due to treatment-related adverse events (AEs) was also considered in this analysis. Data on discontinuation parameters were analyzed by applying a MTC competing risks model appropriate for multinomial distribution of data using WinBUGS. **RESULTS:** Six trials (study follow-up from 24 to 53 weeks) were identified, allowing comparisons of aripiprazole (oral and LAI), risperidone LAI, paliperidone LAI, olanzapine (oral and LAI), haloperidol LAI and placebo. The total patient number was 3402, of which 534 (16%) received aripiprazole. Compared to placebo the risk of relapse was the smallest for aripiprazole LAI (mean hazard ratio [HR]=0.26, 95% confidence interval [CI] 0.12-0.50) and risperidone LAI (HR=0.29, 95% 0.05-0.83). The risk of discontinuation due to AEs was lower than placebo for aripiprazole LAI (HR=0.72) and higher than placebo for the other LAIs (paliperidone LAI: HR=5.08, risperidone LAI: HR=12.06, olanzapine LAI: HR=6.58, haloperidol LAI: HR=4.19). **CONCLUSIONS:** The MTC suggests that aripiprazole LAI is at least as efficacious in the management of relapse prevention as other LAIs with an advantage over other LAIs in terms of discontinuation due to AEs. This study provides support for formulary decision-making in the absence of head-to-head data.

PMH2

RISK OF PSYCHIATRIC AND NEUROLOGICAL DISEASES IN PATIENTS WITH WORKSPACE MOBBING EXPERIENCE IN GERMANY: A RETROSPECTIVE DATABASE ANALYSIS

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OBJECTIVES: In recent years workplace mobbing attracts notice in public and science. Victims of workplace mobbing frequently suffer from depressions, somatic symptoms, may develop alcoholism or other substance abuse disorders and show increased risk of suicidal behavior. The aim of this study was to calculate the number of patients with a workspace mobbing documentation and their diagnosis profile in general practices in Germany between 2003 and 2012 based on the data from a large epidemiological database. **METHODS:** This retrospective study analysed longitudinal routine care data collected by general practitioners in Germany (IMS® Disease Analyzer). Data from patients with notice as workplace mobbing (N=2653) and without such notice (N=2653) from 199 general medical practices in Germany (Disease Analyzer database; 01/2003 to 12/2012) were matched for age (41 ± 13 years), gender (male: 33%), health insurance (private: 5%) and retrospectively analyzed. Odds Ratio (OR; Logistic regression) for depression, anxiety, somatoform disorder, migraine and sleep disorder (follow-up: 3 years) were calculated. **RESULTS:** In 2003, 24 (projected to national level: 2448) patients were documented as mobbing victims; this number continuously increased to 429 (projected to national level: 43758) in 2012. Shares of female patients and mean age have not significantly changed from 2003 till 2012. In workspace mobbing persons there was a increased risk of depression (OR: 4.11, p<0.001), anxiety (OR: 2.76, p<0.001), somatoform disorder (OR: 3.51, p<0.001), migraine (OR: 1.41, p=0.003) and sleep disorder (OR: 2.32, p<0.001). **CONCLUSIONS:** This retrospective database analysis showed that experience of workspace mobbing was associated with increased prevalence of psychiatric and neurological problems. Further research is required to understand this complex issue.

PMH3

POINTS TO CONSIDER IN MULTIREGIONAL TRIALS USING PHQ-9: A META-ANALYSIS ON PHQ-9

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OBJECTIVES: As the cultural adaptation process of PROs (Patient Reported Outcome instruments), every version of PROs should be validated. However, little is known whether those validated PROs are identical in terms of the test performance (operating characteristics). In this study, we investigated PHQ-9 (Patient Health Questionnaire-9 for depression) using the meta-analysis. **METHODS:** We searched PubMed for studies examining diagnostic accuracy of PHQ-9. Then we extracted or retrieved 2 x 2 data from each study and meta-analysis was performed using Bivariate model (Reitsma et al. 2005). As the language versions of PHQ-9 and regions where the studies were conducted would be potential confounding factors, we performed meta-regression. Bivariate meta-analysis of the subgroup (region, language) was explored. **RESULTS:** Twenty-eight studies met our inclusion criteria. Univariate meta-regression showed that all the covariates assessed such as language, region significantly contributed to the heterogeneity of sensitivity (I^2=82.7) and specificity (I^2=92.5) among the studies. Meta-analysis of subgroup of the regions and languages was made using bivariate model; studies conducted in North America (6 studies), Europe (13 studies), or Asia & others (9 studies); LogitSe of North America, Europe and Asia& other were 1.66, 1.45, and 1.48, respectively. Logit Sp of these regions was 1.87, 1.90 and 2.22, respectively. **CONCLUSIONS:** Results suggest that operational characteristics would influenced by the regions, language version of PHQ-9. Therefore, when considering a multiregional study using PHQ-9 as screening tool, there would be a chance of some imbalance among regions. Therefore, before initiation of the clinical studies, efforts need to minimize the heterogeneity of the definite diagnosis, e.g. training to the investigators, or central diagnosis.

PMH4

RESULTS FROM THE "AUTOR" STUDY, A EUROPEAN OBSERVATIONAL STUDY IN PEDIATRIC PATIENTS WITH ATTENTION-DEFICIT/HYPERACTIVITY DISORDER

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OBJECTIVES: To investigate factors associated with changes in attention-deficit/hyperactivity disorder (ADHD) symptom severity and quality of life (QoL) in patients who were responders and stable on their pharmacotherapy at study entry. **METHODS:** "AUTOR" is a European prospective, observational study investigating factors associated with ADHD severity changes during a 2-year follow-up period in patients aged 6-17 years. At baseline, patients had received the same pharmacotherapy for 3-8 months and had a Clinical Global Impression (CGI)-ADHD-Severity score of mild or lower and a CGI-ADHD-improvement score of improved/very much improved since treatment initiation. Data were collected at naturally occurring visits coinciding with observation windows (postbaseline): 0, 3, 6, 9, 12, 18, and 24 months, and ±6 weeks. ADHD symptom severity worsening was defined as a ≥2-point increase from baseline in CGI-ADHD-Severity score. The Child Health Profile-Child Edition (CHIP-CE) was used to measure QoL. Multivariate logistic regression was used to assess the association of different factors with changes in ADHD severity at any time postbaseline. Mixed-model repeated measures (MMRM) regression was used to estimate adjusted differences between treatments. Propensity scoring was used to adjust for imbalanced covariates before treatment comparisons. **RESULTS:** Data were analyzed from 704 patients (mean [standard